Cardiovascular Disease
Cardiovascular disease: heart & blood vessels (vascular)

1. > 70 million people in US
2. Economic cost: $300 billion (2001)
3. #1 killer
4. **385,000** coronary heart disease deaths - 2004 (**1055/day**)
5. Stroke- related vascular disease: #3 killer
• Heart disease: a man’s disease?
• #1 killer American women: more than men
Underlying process:

Athere = porridge (Greek)
Sklerosis = hardness (Greek)

Arteriosclerosis: general- hardening of arteries

Atherosclerosis: arteries narrowed by fatty deposits (plaques)
Do you have atherosclerosis?  YES

• All humans have this disease (susceptible)
• Dogs/rats: resistant
• Going on slowly, quietly in you now
• Deposits throughout your arteries: Heart, brain, neck, arms/legs
• Arms: feel- small hard “pipes” (peripheral artery disease)
• Coronary = coronarius (Latin): a crown or circle
• Coronary circulation: encircles heart
• Coronary Artery Disease
Peripheral Artery Disease
55 year old woman
Awoke: numbness & weakness: both legs
Smoker, ↑ blood lipids
Angiogram: *blocked* lower aorta
Treatment: antiplatelet, statin therapy, stop smoking, exercise
OK at next hospital visit
When does atherosclerosis start?

- **Children**: see artery **thickenings** & “**fatty streaks**” (5-12 years)
- **Early lesions** (injury): coronary arteries & aorta: seen sometimes-newborn babies & fetuses
- **Suggests**: prenatal environment-role in atherosclerosis
Juvenile intimal thickening

Juvenile fatty streaks and diffuse sudanophilia

Transitional fatty streaks in a young adult
A Pediatric Disease

Because many little hearts are destined for a big problem...
• Many doctors: atherosclerosis is a “pediatric disease”: begin early prevention
• 2008 AHA study: Thickening in arteries: obese 10 year olds = 45 year old adult
• “You are as old as you arteries are”
Evolution of atherosclerosis:

Early **thickenings**

- fatty streak
- fibrous plaque

- advanced, complicated lesion

(vulnerable to burst)
• American soldiers (19-20) killed:
  Korean War
  Viet Nam War
• Autopsies: extensive atherosclerosis

The deterioration of a normal artery (left) is seen as atherosclerosis develops and begins depositing fatty substances and roughening the channel lining (center) until a clot forms (right) and plugs the artery to deprive the heart muscle of vital blood which results in heart attack.
• Thomas Herrion: 23 year old, 6’ 3”, 315 pound lineman: San Francisco 49ers
• 2005: died suddenly after exhibition game
• Significant blockage: right coronary artery
• Enlarged heart; no drug abuse
1984 Stormie Jones: 6 year old girl
Texas

- Wartlike bumps: elbows, knuckles, knees, toes: started: age 3 months
• Bumps: **cholesterol deposits** under skin
• Sign of: Familial Hypercholesterolemia
• LDL cholesterol: 9X normal
• Genetic defect: 2 bad copies of gene → LDL receptor
• 1 in million people
• LDL receptors: membranes of liver/other cells
• Like “magnets” pull LDL out of blood
• No receptors: LDL stays in blood atherosclerosis
• October 12, 1984: **heart attack**
• Days later: chest pains, 2 bypass operations - no help
• Last ditch effort: 15 hour operation - transplant heart & liver
Why double transplant?

• She received heart without clogged arteries

• She received good liver with **active** LDL receptors: help lower blood cholesterol
• Stormie Jones helped Drs. Michael Brown & Joseph Goldstein (UT) discover LDL receptor defect
• Nobel prize 1985
In patients with multiple risk factors for heart disease,

**Lipitor** reduces risk of heart attack by **36%**

If you have risk factors such as family history, high blood pressure, age, low HDL (‘good’ cholesterol) or smoking.

**DR. ROBERT JARVIK**

~Inventor of the Jarvik Artificial Heart and Lipitor User
First statin isolated from fungus (Penicillium citrinum)
Atherosclerosis: What are its symptoms?

- None: early on
- Later: artery clogged in heart: heart attack
• **Myocardium**- heart muscle
• **Infarct**: tissue death/no blood supply
• **MI**

Uncontrolled high blood pressure increases the risk of...

**Heart attack**

- One of the arteries supplying the heart with blood can become *completely* blocked.
- The part of the heart muscle that doesn’t get blood dies from lack of oxygen. This can be life-threatening.

Medical term: Myocardial infarction (MI)
Heart attack: Warning signs

• Heavy pressure, fullness, squeezing pain in center of chest
• Pain may spread: arms, back, neck, jaw, or stomach
• Cold sweat
• Nausea and vomiting
• Lightheadedness
Heart Attack Pain: may spread
Heart Disease: Women vs. Men

- Men affected by heart disease 10 years earlier than women
• Until puberty: boys & girls same HDL levels

• At puberty: boys ↓ HDL
  girls ↑ HDL ↓ LDL
  (estrogen)

With menopause (35-58):
  ↓ estrogen ↑ weight ↑ heart risk
Men more likely: blockages: big coronary arteries: crushing chest pains
Women: more common: “microvascular disease”- thickening, stiffening of smaller arterioles- supply heart

• Don’t dilate very well
• Heart muscle-starved O2
• Chest pains, abnormal stress test
A Hidden Risk

While an angiogram, in which dye is injected into the coronary arteries, helps doctors to determine whether the blockages are forming in the larger vessels of the heart, the test does not reveal the smaller vessels, microvasculature. Blockages in these small vessels, which seem to be more common in women, can become an undetected threat.

Typical Angiogram

Larger vessels stand out while smaller ones, because of their microscopic size and the motion of the heart, are lost in a blur.

Microvasculature

Other imaging techniques used on hearts removed from the body reveal the vast network of vessels unseen by the angiogram. This image shows the microvessels in a pig’s heart.
• Standard **angiogram**: inject dye, X-Ray coronary arteries (big)

• Only **1/3** women show big blockages

*Angiogram of a heart showing blockage of the right coronary artery.*
• Rest of heart disease: missed in angiograms of women

• 3 million American women- this type of heart disease: “coronary microvascular syndrome”

• Further tests: women: arterioles don’t dilate, ↓ blood flow
Women’s Warning Signs

- Chest discomfort
- Mild/severe pressure, fullness, or pain: center of chest
- Discomfort: arms, back, neck, jaw, stomach
- Shortness breath
- Nausea, light headedness or sudden cold sweat
- Extreme fatigue
Angina: may be warning sign: heart attack on the way

- Angina from “angere” (Latin): choke
Angina:

1. Pain: tight, crushing, suffocating, beneath breastbone
2. Heaviness/tightness - chest
3. Occurs: exercise (exertion), emotional stress
4. Lasts: 2-15 minutes - goes away
Angina cause:

1. Spasm- coronary arteries- insufficient blood to heart muscle = myocardial ischemia

2. Result of: atherosclerosis- coronary arteries
Heart disease: Who’s at risk?

• Framingham Heart Study (1948): followed participants → today

• Identify “risk factors”

• Risk factors:

  Having 1 = BAD

  2 = Worse

  3 = Terrible
Risk Factors: **Uncontrollable**

1. **Sex:** Increased risk: men $\geq 45$
   women $\geq 55$

2. **Family history:** increased risk if:
   Male relative- heart disease before age **55**
   Female relative- heart disease before age **65**
Risk Factors: Uncontrollable

3. ↑ Age ↑ Risk 4/5 people die of heart disease > 65

The older you get, the more your heart needs protection
Risk Factors: Uncontrollable

4. Genetics ↑ Risk
   
   A) African Americans *(high blood pressure)*
   
   B) Mexican Americans, Native Americans, Hawaiians *(diabetes & obesity)*
Risk Factors: **Controllable**

5. Cigarette smoking
Tobacco Smoke

1. \( \downarrow \) HDL
2. **Platelets sticky**: blood clot
3. CO: reduce blood oxygen to heart
4. **Nicotine**: arterial cell toxin
5. \( \uparrow \) adrenaline, heart rate, blood pressure, arrhythmias
6. Heart works harder but can’t get enough oxygen (CO)
7. Mutagens, carcinogens, allergens, radioactivity
8. Nicotine: addictive signs- 2 days start smoking: young people
2008 Dutch Study
- Pregnant women who **smoked**
- Their children years later (age 28)
- ↑ Thickness carotid arteries
6. Blood fats (increased risk)

- LDL cholesterol $> 100$ mg
- HDL cholesterol $< 40$ mg
- Total cholesterol $> 200$ mg
- Triglycerides: $> 150$ mg

*HDL: the protective lipoprotein*

HDL (high-density lipoprotein) has been called the "good" lipoprotein because unlike LDL (low-density lipoprotein), which promotes fatty deposits in the blood vessels, HDL helps eliminate cholesterol from the body. Because of this, researchers have noted that persons with higher levels of HDL have a lower rate of heart disease.
Cholesterol

The Good
HDL

and

The Bad
LDL
• Newborn babies: LDL 40-50 mg
• Populations: low risk, low fat diets: LDL < 100 mg throughout life
• Brown/Goldstein: “keep LDL as low as possible beginning as child”
LDL vs. HDL: Balance is important
Bottom line:
Keep **LDL low** and **HDL high**
7. High Blood Pressure: 

≥ 140/90
8. **Diabetes**: fasting blood sugar: 

≥ 126 milligrams
9. **Obesity**

**Overweight**

BMI > 25

and

waist circumference:

> 35 inches - women

> 40 inches - men
10. **Sedentary Lifestyle**
   *(inactivity)*
Boston Irish Brothers Study

• Large study: 1 brother immigrated to Boston, other stayed Ireland
• Ireland brother ate $\frac{1}{4}$ more food/day but weighed 10 pounds less
• Ireland brothers: less heart disease
• Ireland brothers: more exercise/physical activity- compensated for excess food
11. Diet & Coronary Risk

↑ Saturated fat, trans fat, cholesterol

↓ Fiber, fruits, vegetables
Other risk factors

• ↑ C Reactive Protein ↑ Risk
  Indication of inflammation in body (arteries)

• ↑ Blood homocysteine ↑ Risk
  (amino acid)
  Vitamins B6, B12, folic acid lower homocysteine
  Foods: fortified grains (cereals, breads), fruits, veggies
Other risk factors

Stress
Stress: Job, society, school, peers

1. Some people: prone to emotional stress - worsen blood pressure, angina

2. Long-term adrenaline: heart rate, blood pressure, blood glucose

3. Stress & overeating, smoking
Personality Type

• Type A: Coronary prone
Type A:

Time urgency, impatient, competitive, aggressive

Subtype: hostile, cynical, increased adrenaline stress response: ↑risk
Type B: more relaxed, less time conscious: ↓ risk

2006 Dutch “Outlook on life” study: men 64-84 followed for 15 years
“I still expect much from life”
“I am still full of plans”
50% lower risk dying heart disease
How does atherosclerosis begin?

Atherosclerosis: accumulation: lipids, protein, calcium, scar tissue in arteries: atherosclerotic plaque

Artery: ↓ elastic (hardened), blood flow eventually blocked
Atherosclerosis Sequence

1. Injury (insult) to inner lining of artery wall
Injury: Different factors

- LDL (oxidized)
- Glucose
- Homocysteine
- Blood pressure
- Free radicals - cigarette smoke
- Diabetes
- Infection - virus: Herpes virus
detected in atherosclerotic plaque
2. Inner lining: develops openings

- LDL moves in from blood

- Platelets attach to injured lining: release *growth factors*

- Smooth muscle cells → divide: thickening (like cancer)
HOW CHOLESTEROL CAN CLOG YOUR ARTERIES

1. Atherosclerosis is believed to begin when the lining of an artery, the endothelium, is damaged by factors including high blood pressure, elevated cholesterol levels or infection.

2. Two forms of blood cells accumulate in the damaged vessel wall: platelets and macrophages. The latter become foam cells as they gorge on cholesterol. When they burst, a fatty deposit forms.

3. Smooth muscle cells migrate from the layer below the endothelium and multiply wildly. Over a period of years, this proliferating jumble blocks the flow of blood, leading to a heart attack or stroke.
3. LDL inside artery - *oxidized*: dangerous
   - Triggers *inflammation*
   - White cells in blood → artery wall macrophages
   - Gobble up oxidized LDL → bag of fat: *foam cells*
   - Foam cells burst: release fat *fatty streak*
4. Injury (lesion) grows → plaque
• Cap (cover) of protein forms: **fibrous plaque**
• Attempt to “wall off” damaged artery
• Immune cells in plaque break down cap: ruptures
5. **Clot** forms on roughened surface

- **Thrombosis (thrombus)**
- Partially blocked artery **completely blocked**
- Heart attack: **myocardial infarction**
Heart attacks: more common morning, on birthdays.
6. Damage to heart muscle triggers: abnormal heart rhythms (*cardiac arrhythmias*)

- Most dangerous: *ventricular fibrillation*
- Heart quivers, stops pumping
- “Bag of worms”
- Blood → brain, other organs
Ventricular fibrillation - loss of consciousness, death quickly

A. Do CPR

B. Shock heart back into normal rhythm: defibrillator (paddles) - airplanes, airports
Heart Attack

Classic “Hollywood heart attack”—person clutching chest
Heart Attack

- Not always true
- Sometimes-less distinct symptoms (women & elderly)
- Discomfort/pressure- chest
- Exhaustion: just walking across room
- Break out: cold sweat
- Diabetics: sudden extreme fatigue: “silent heart attacks” (scar tissue)
• Heart attack may last 4-6 hours
• With each passing minute: heart tissue → no O2 → dies
• If conscious: suggestion- “chew” on aspirin- prevent further clotting/help blood flow
Regardless of type:

- **Every minute counts**
- "Golden hour": "Time is muscle"
- ~ 1 hour:
  - get arteries open
  - prevent permanent heart damage

![Critical Timing Graph]

*Source: Mayo Clinic College of Medicine*
Problem: \( \frac{1}{2} \) people with heart attacks don’t call ambulance
MI: 2 treatments at hospital

1. Clot buster: tissue plasminogen activator (tpa): not perfect - only opens 60-70% blockages

2. Balloon angioplasty + stent (stainless steel mesh) - keeps artery open
Stents

Stent is positioned in coronary artery ...

... Balloon is then inflated ...

... Stent keeps artery open.

Catheter is inserted into femoral artery.
Angioplasty Procedures

Narrowed coronary artery

Balloon angioplasty

Atherosclerotic plaques

Stent
Following angioplasty, a stent is often placed in the artery to prevent re-narrowing.
Heart Disease: How do you detect it?

- Electrocardiogram (ECG): look for abnormal rhythms
Cardiac stress test: treadmill + ECG

He denies symptoms of ischemic disease, but his stress ECG is positive.
• **Coronary angiography**: gold standard

Catheter ➔ coronary arteries ➔ blockages ➔ X-Ray movies ➔ dye
Coronary Angiogram
53 year old man
Severe blockage
How do you treat heart disease?

1. Healthy diet
2. Exercise
3. Stop smoking
4. Medications:
   A) Statins
   B) Bile acid-binding resins (sequestrants)

Both deplete liver-cholesterol

↑ Liver LDL receptors ↓ blood LDL
C) **Aspirin**- baby aspirin (81 mg): may prevent clots, protect against heart attack/stroke

Higher dose—may be harmful: GI bleeding
D) Niacin - B vitamin: ↓ LDL ↑ HDL

5. Coronary angioplasty + stent
6. **Coronary Artery Bypass Graft (CABG):** improve blood flow

   A) Use vein from leg/arm or
   B) Mammary artery grafted around blocked artery

- President Clinton: multiple bypasses
Dietary Factors: to reduce progression of atherosclerosis

1. ↑ Whole grains ↓ Heart risk
   Contain: fiber, vitamins, minerals, antioxidants (LDL), phytochemicals
   Also control blood glucose, blood pressure, prevent obesity
2. **↑ Simple sugars**
   
   **↑ Blood triglycerides**
   
   **↑ Heart risk**

Limit: cookies, high sugar drinks, snacks, candy
3. **Soluble fiber** ↓ **Heart Risk**
   - cholesterol & bile acid absorption - intestine: ↓ LDL

**Soluble fiber sources:**
- Oat bran, oats, oatmeal, peas, beans, apples, flaxseed, psyllium (Metamucil), pears, peaches, plums, oranges, broccoli, Brussels sprouts
4. \(\uparrow\) Cholesterol \(\uparrow\) Heart Risk

20\% \text{ cholesterol} = \text{ food}

80\% \text{ cholesterol} = \text{ made in your body (liver)}
5. ↑ Total Fat ↑ Heart Risk

Exceptions:

A) Greenland Inuits:
   ↑ omega 3 fats (fish)
   ↓ heart disease

B) Mediterranean diet: high monounsaturated fats, whole grains, fruits/veggies, wine, low animal foods ↓ heart disease
6. ↑Saturated fat ↑ Heart risk
Meats, dairy products (whole milk, cheese, ice cream), prepared (frozen) foods

↓ LDL receptors - liver  ↑ LDL

Limit: 20 grams/day (< 10% calories)
Where the saturated fat is at

- **Animal fat:**
  - Beef: 50%
  - Chicken: 30%
  - Pork: 39%

- **Tropical oils**
  - Coconut: 87%
  - Palm oil: 49%
  - Palm kernel oil: 82%
Low saturated fat:

- **Vegetable oils**
  - Canola: 6%
  - Corn: 13%
  - Cottonseed: 26%
  - Olive: 13%
  - Peanut: 17%
  - Safflower: 9%
  - Sesame: 14%
  - Soybean: 15%
  - Sunflower: 10%
7. ↑ Trans fat ↑ Heart risk
   ("partially hydrogenated")

   ↑ LDL ↓ HDL

   Keep as low as possible in diet
8. Polyunsaturated fat ↑ Heart risk ↓

Veggies, nuts, corn, soybean, safflower, sunflower oils, soft/liquid margarines

↓ LDL but also slight ↓ HDL
9. **↑ Omega 3 fats**

**↓ Heart risk**

Fish, fish oil, flaxseed, soybean oil, canola oil, walnuts

Eat fish: **2-3 times/week**

↓ Triglycerides  ↓ LDL  ↑ HDL

**Good heart rhythms**
10. **↑** Monounsaturated fat  **↓** Heart risk

Olive oil, canola oil, high “oleic” safflower & sunflower oils, nuts

↓ Blood pressure, ↓ LDL  ↓ LDL oxidation

Polys + monos = **45 grams/day**
11. ↑ B Vitamins ↓ Heart Risk
Vitamins B6, B12 & folic acid

Keep homocysteine low

↑ homocysteine  ↑ atherosclerosis

Sources: enriched grains, fruits, veggies
12. **Moderate alcohol**

**↓ Heart risk**

**↑ HDL**  **↓ Blood clotting**

Ethinol: wine, beer, mixed drinks

**Red wine: polyphenols** (phytochemicals): **↓ LDL oxidation**

Moderate limit: 2 drinks/day men

1 drink/day women
13. **Soy products**

Soy protein, phytoestrogens

$\downarrow$ LDL may be $\uparrow$ HDL

Cholesterol-lowering effect - not as dramatic as once thought
14. **Plant sterols/stanols**

↓ Heart risk

Reduce cholesterol absorption - intestine

↓ LDL

Small amounts: fruits, veggies, nuts, seeds, cereals, peas, beans, vegetable oils

Now added to: salad dressings, OJ, **margarines** (Benecol, Take Control)
“I just lowered my cholesterol by 11%.*
Now I’m sittin’ pretty.”

Maria Angeles, mother of 3

Maria Angeles not only significantly lowered her cholesterol in just three weeks—she did it the natural way.

Every day she used delicious Take Control spread. It contains natural soybean extract clinically proven to help your body reduce LDL or “bad” cholesterol.

In fact, a recent study showed that enjoying Take Control spread twice a day, plus changing to a diet low in cholesterol and saturated fat, can lower LDL by 17%! That’s why no other spread is more effective at lowering “bad” cholesterol. And this may actually reduce the risk of heart disease.

It’s only natural that Maria Angeles got such spectacular results.

Make your own Take Control spread today.
In a national survey of 310 cardiologists, 4 out of 5 endorsed Promise® SuperShots® for cholesterol, based on nutritional information.

These delicious fruit and yogurt-flavored blends contain natural plant sterols, ingredients clinically proven to help remove cholesterol from your body.

Enjoy daily with meals as part of a diet low in saturated fat and cholesterol, and you could see reduced cholesterol levels.

For more information on plant sterols, go to WebMD.

TRY ALL FOUR FRUIT FLAVORS!
Strawberry, Peach, Raspberry, Blueberry

Foods containing at least 0.4 grams per serving of plant sterols, eaten twice a day with meals for a daily total intake of at least 0.8 grams, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. A serving of this product provides 2 grams of plant sterols. ©2008 Uniliver
15. **Caffeinated beverages**

Elderly $\uparrow$ caffeinated drinks $\downarrow$ heart disease death risk

But people with **MI** in hospitals

High coffee intake: risk ventricular arrhythmias
16. **DASH Diet**

↓ **Blood pressure**

↓ **Heart risk**

**Eat more**: Fruits, veggies, whole grains, low-fat dairy products, poultry, fish, nuts

**Eat less**: Total fat, red meat, sweets, sugary drinks
17. **Meal frequency**

NIH High Blood Pressure in Adults Expert Panel

- Eat throughout day
- **Smaller** meals & snacks *(healthy, low calorie)*
- Instead of: 1 large meal in evening, before bed
18. **Activity/exercise**

- Be active most days of week: **30-60 minutes**
- Maintain healthy body weight
- 2007 study: people use **pedometers**: more motivated
- ↓ BMI  ↓ Blood Pressure
- +2000 steps/day = 1 mile
19. **Antioxidants**

- **Inconsistent results**
- Some studies: ↑ fruits/veggies ↓ heart disease
- ↑ Vitamin E- smokers ↓ coronary deaths
- Other studies: Vitamin E: people at risk heart attack/stroke: **No effect**; ditto: Vitamin C, Beta carotene
Do Hershey’s Kisses lower blood pressure?
• German study 2007:
• People- blood pressure: **147/86**
• Ate: 6 grams white or dark chocolate (equal in amount to **1.5 Hershey’s Kisses** per day)
• **Dark** chocolate from cocoa- rich in **flavonoids**
• After 18 weeks: systolic ↓ 3 points (dark)  
  diastolic ↓ 2 points
Flavonoids:
1. Decrease LDL oxidation
2. Lower LDL, raise HDL
3. Vasodilation
4. Decrease inflammation
5. Decrease blood pressure
6. Decrease platelet clumping
7. Increase insulin sensitivity
Flavonoids in black tea

- Netherlands study
- > 3 cups black tea/day
- ↓ heart attack rate

**Green Tea** (catechins)

- ↓ CRP (inflammation)
- Antioxidant abilities
Flavonoids -other sources:
Green/black tea, cherries, purple grapes, blackberries, raspberries, blueberries, cranberries, plums, bran, red apples, pears, red wine, strawberries, grapefruit, prunes

*Organic tomatoes higher in flavonoids
• Problems: Current way manufacturers make cocoa & chocolate: destroys most flavonoids
• Chocolate: high in calories & fat